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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,122	09/19/2003	Reiner Laus	20642/1203635-US2	8703

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,122	LAUS ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,10,12 and 21-30* is/are pending in the application.

4a) Of the above claim(s) *21-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4, 10, 12 and 21-30 are all the pending claims in this application.

2. Claims 2, 3, 5-9, 11 and 13-20 were canceled and Claims 1 and 10 were amended in the Response of 1/18/07. Support for the amendments to the body of Claim 1 to include limitations from cancelled claims 6, 7, 16 and 20 is acknowledged and entered.

3. Applicants did not discuss the original written support for transitional language, "consisting essentially of", in amended Claim 1 in their Response of 1/18/07 nor provide an example of an embodiment falling within the claim scope. Applicant's representative, Peter Dehlinger, was contacted by the Examiner on 4/16/07 and invited to discuss the intended meaning of the claim scope for purposes of advancing the examination. No reply was returned.

4. Claims 21-30 are withdrawn from examination.

5. Claims 1, 4, 10 and 12 are all the pending claims under examination.

Examiner's Decision on Petition to Correct Inventorship

6. The request to correct the inventorship of this nonprovisional application under 37 CFR 1.48(a) is granted. Applicants' Petition of 1/18/07 (executed by Peter Dehlinger) including copies of the following documents have been considered and entered:

a) Petition to Correct Inventorship (executed by Gary Miles)

b) Statement Under 37 C.F.R. §1.32(B)(2) by Inventor Small (executed by Eric Small)

c) Statement Under 37 C.F.R. §1.32(B)(2) by Inventor Rini (executed by Brian Rini)

d) Request for Corrected Filing Receipt (executed by Gary Miles)

e) Filing receipt with hand-written annotations

f) Date-stamped filing receipt of 4/26/04

g) Executed Oath/Declaration

Applicants amended Application Data Sheet, which lists the named inventors for this application has also been considered and entered.

Withdrawal of Objections

Sequence Listing

7. The objection to the originally filed Sequence Listing as listing the names of Small and Rini is withdrawn in view of the revised Sequence Listing to delete the non-inventor names.

Specification

8. The objection to the specification for the improper use of the trademark for "PCR" is withdrawn in view of the new paragraph at p. 26, lines 11-18; p. 2 of the Reply of 1/18/07.

9. The objection to the abstract and specification for including the attorney docket no. of each of the pages is withdrawn in view of the amendment and Applicant's instructions on p. 2 of the Reply of 1/18/07.

Claims

10. The objections to Claim 5 as being drawn to non-elected subject matter for species of cancers; and Claims 5 and 6 as drawn to prostate cancer and reciting duplicate subject matter is withdrawn and rendered moot in view of the cancellation of the claims.

Withdrawal of Rejections

Claims - 35 USC § 112, second paragraph

11. The rejection of Claim 2 as being indefinite for reciting a "tumor-specific antigen" is withdrawn in view of the cancelled claim. Applicant's comments on p. 9 under section III of the Response of 1/18/07 are acknowledged.

Claims - 35 USC § 112, first paragraph

Written Description

12. The rejection of Claims 13-15 and 17-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reciting an N- or C-terminal moiety having at least 70%, 80% or 90% sequence identity with the amino acid sequence of SEQ ID NO:1 (huPAP) or 3 (huGM-CSF), is withdrawn and rendered moot in view of the cancelled claims. Applicant's comments on p. 9 under section IV of the Response of 1/18/07 are acknowledged.

Enablement

13. The rejection of Claims 2, 3, 5-9, 11, 13-15 and 17-19 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn and moot in view of the cancelled claims.

Claims - 35 USC § 102

14. The rejection of Claims 2, 3, 5-9, 11, 16 and 20 under 35 U.S.C. 102(b) as being anticipated by Small et al. (J. Clin. Oncol. 18:3894-3903 (2000)) is withdrawn and rendered moot in view of the cancelled claims.

15. The rejection of Claims 2, 3, 5-9 and 11 under 35 U.S.C. 102(b) as being anticipated by Burch et al. (Clin. Cancer Research 6:2175-2182 (June 2000)) is withdrawn and rendered moot in view of the cancelled claims.

Claims - 35 USC § 103

16. The rejection of Claims 2, 3, 5-9, 11, 16 and 20 under 35 U.S.C. 103(a) as being unpatenable over Laus et al. (USPN 6,210,662, published April 3, 2001, filed June 24, 1999) in view of Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) is withdrawn and rendered moot in view of the cancelled claims.

17. The rejection of Claims 2, 3, 5-9, 11, 16 and 20 under 35 U.S.C. 103(a) as being unpatenable over Fikes et al. (US20040037843, published February 26, 2004, filed

December 20, 2000) in view Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) is withdrawn and rendered moot in view of the cancelled claims.

Objections Maintained

Information Disclosure Statement

18. Applicants' IDS of January 12, 2004 was identified as being misfiled with the instant application. The Examiner requested that Applicant's expunge the document from the prosecution file. Applicants have not commented on the IDS in their Reply or provided the Office with any instructions, thus the objection to the IDS is maintained.

Specification

19. The objection to the specification for the improper use of trademarks is maintained for ISOLEX (new paragraph at p. 34, lines 9-15; p. 2 of the Reply of 1/18/97) and AVASTIN (new paragraph at p. 35, lines 20-23; pp. 2-3 of the Reply of 1/18/07). Applicants have deleted the trademark designations and not provided the generic definitions for these products.

Applicants are advised to carefully check the entire specification for any other trademarks or tradenames that may not be properly identified.

Rejections Maintained

Claims - 35 USC §112, first paragraph

Enablement

20. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 112, first paragraph, as not being enabled for making or using a immunotherapeutic composition "consisting essentially of" an APC from a prostatic cancer patient with a Gleason score of 7 or less and stimulated *ex vivo* with a fusion protein composed of huPAP and huGM-CSF where the huPAP and huGM-CSF "have" SEQ ID NOS: 1 and 3, respectively, is maintained.

Applicants allege on p. 9 under section V of the Response of 1/18/07 "the inclusion of the above limitations to amended claim 1 is effective to overcome this limitation." Applicant's allegations and the amendment of Claim 1 to recite "consisting essentially of" language are not found persuasive.

The Examiner submits that despite the amendment of Claim 1 to introduce the limitations for a prostate cancer, a Gleason score and a fusion protein "composed" of huPAP and huGM-CSF each "having" SEQ ID NO:1 and 3, respectively, the introduction of "consisting essentially of" language does not specifically exclude other elements within the composition or other elements occurring within the structure of the fusion protein, which materially effect the basic and novel characteristics of the invention , i.e., the APC and the fusion protein. In other words, the language does not exclude from the fusion protein the presence of sequences other than those coding for huPAP and huGM-CSF, and which can otherwise affect the properties of the fusion protein. Additionally, other elements of PAP and GM-CSF which can impart or effect the

structural or functional properties of the molecules themselves can include, for example, a) bioeffecting regions in the full length sequence for the huPAP and/or huGM/CSF proteins, i.e., N-terminal leader sequence or transmembrane domain, other than intended APC immunostimulatory domains, and/or b) a linker peptide in the fusion protein itself.

For example, the specification specifically teaches at p. 17, line 22- p. 18, line 6, a PAP/GM-CSF fusion protein of SEQ ID NO:5 as occurring between a 386 amino acid portion of PAP at the N-terminus and a 127 amino acid portion of GM-CSF at the C-terminus, with a two amino acid peptide linker having the sequence gly-ser occurring between the N- and C-terminal moieties. Notably, SEQ ID NO:5 is only 144 amino acids in length in the original and revised Sequence Listings. Applicants are requested to address this discrepancy between the specification and SEQ ID NO:5 of the Sequence Listing. Further, the specification teaches PAP/GM-CSF fusion proteins comprising sequence variations within the amino acid sequence of the PAP and GM/CSF moieties. All of the working examples in the specification disclose the PAP/GM-CSF fusion (PA20224) indicated as comprising SEQ ID NO:5 (see Example 1).

Linker peptides discussed more specifically on pp. 18-19, are taught as being optional (see line 26), and that the linkers "are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference." From this disclosure, it is not even clear whether a peptide linker would be required for the instant claimed

fusion protein having the full length huPAP of SEQ ID NO:1 and the full length huGM-CSF having SEQ ID NO:3.

Thus based on the foregoing analysis, the Examiner submits that the claimed immunostimulatory composition is not enabled because the claims encompass other elements that potentially materially effect the basic and novel characteristics of the composition. (see *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, (Fed. Cir. 1997) "For an inserted cDNA having a DNA sequence coding for human [PI], the word "having" still permitted inclusion of other moieties. The claims were again rejected based upon the same references and in a later requirement that the word "having" be changed to "consisting essentially of", the examiner allowed the claims, noting that the "consisting essentially of" language "excludes from the cDNA the presence of sequences other than those coding for PI.")

Claims - 35 USC § 102

21. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 102(b) as being anticipated by Small et al. (J. Clin. Oncol. 18:3894-3903 (2000); hereinafter referred to as "Small") is maintained and as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)).

Applicant's arguments filed in the Response of 1/18/07 on p. 11 under section VI, subsection C have been fully considered but they are not persuasive. Applicants allege that Small does not mention the Gleason score of the patients enrolled in the study, nor is there any evidence that any of the patients were Gleason 7 or less.

The Examiner submits that absent a showing of any difference, a Gleason score of 7 or less would be inherent to the population of patients described in the Small reference. As evidenced by Ahmed, "moderately differentiated" prostatic tumors would have Gleason's scores of 5, 6 or 7, thus the immunostimulatory composition of Small is deemed to be the same as the instant claimed immunostimulatory composition, since although Small does not teach the Gleason score of the tumor, Ahmed teaches "moderately differentiated" tumors would be recognized as having Gleason's scores of 5, 6 or 7.

22. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 102(b) as being anticipated by Burch et al. (Clin. Cancer Research 6:2175-2182 (June 2000); hereinafter referred to as "Burch") is maintained and as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)).

Applicant's arguments filed in the Response of 1/18/07 on p. 11 under section VI, subsection D have been fully considered but they are not persuasive. Applicants allege that Burch does not mention the Gleason score of the patients enrolled in the study, nor is there any evidence that any of the patients were Gleason 7 or less.

The Examiner submits that absent a showing of any difference, a Gleason score of 7 or less would be inherent to the population of patients described in the Burch reference. As evidenced by Ahmed, "moderately differentiated" prostatic tumors would have Gleason's scores of 5, 6 or 7, thus the immunostimulatory composition of Burch is deemed to be the same as the instant claimed immunostimulatory composition, since

although Burch does not teach the Gleason score of the tumor, Ahmed teaches "moderately differentiated" tumors would be recognized as having Gleason's scores of 5, 6 or 7.

Claims - 35 USC § 103

23. The rejection of Claims 1, 4, 10 and 12 under 35 U.S.C. 103(a) as being unpatenable over Laus et al. (USPN 6,210,662, published April 3, 2001, filed June 24, 1999) in view of Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) is maintained and as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)).

Applicant's arguments filed in the Response of 1/18/07 on pp. 11-13 under section VII, subsections B and C have been fully considered but they are not persuasive. Applicants allege that Laus does not teach using APCs from a prostate-cancer patient having a moderate to well differentiated cancer grade and Gleason score of 7 or less.

The Examiner submits that both Laus and Smith disclose the immunostimulatory composition with APCs derived from prostate cancer patients, and that Smith teaches the prostate cancers being moderately to well differentiated in grade in the subject population. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, and as discussed supra under the rejection for the claims over the

Small reference, the Gleason score of 7 or less would be inherent to the population as evidenced by Ahmed.

24. The rejection of Claims 1, 4, 10 and 12 under under 35 U.S.C. 103(a) as being unpatenable over Fikes et al. (US20040037843, published February 26, 2004, filed December 20, 2000) in view Small et al. (J. Clin. Oncol. 18:3894-3903 (December 2000)) is maintained and as evidenced by Ahmed et al. (J. Pak. Med. Assoc. 52:54-56 (2002)).

Applicant's arguments filed in the Response of 1/18/07 on pp. 11-13 under section VII, subsections B and C have been fully considered but they are not persuasive. Applicants allege that Fikes does not teach using APCs from a prostate-cancer patient having a moderate to well differentiated cancer grade and Gleason score of 7 or less.

The Examiner submits that both Fikes and Smith disclose the immunostimulatory composition with APCs derived from prostate cancer patients, and that Smith teaches the prostate cancers being moderately to well differentiated in grade in the subject population. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, and as discussed supra under the rejection for the claims over the

Small reference, the Gleason score of 7 or less would be inherent to the population as evidenced by Ahmed.

Conclusion

25. No claims are allowed.

26. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SUPERVISORY PATENT EXAMINER